consisting of SEQ. ID. No. 2, SEQ. ID. No. 3, SEQ. ID. No. 4, SEQ. ID. No. 5, SEQ. ID. No. 6, SEQ. ID. No. 7, SEQ. ID. No. 8, SEQ. ID. No. 9, SEQ. ID. No. 10, and SEQ. ID. No. 12.

18. (Once amended) The isolated nucleic acid of claim [1]45, wherein [the subsequence]said nucleic acid specifically hybridizes under stringent conditions to SEQ. ID. No. 10.

19. (Once amended) The isolated nucleic acid of claim 18, wherein [the subsequence] said nucleic acid is SEQ. ID. No. 10.

Please add new claim 45 as follows:

45. (New) The isolated nucleic acid of claim 1 wherein said nucleic acid has a length of at least 50 nucleotides.

REMARKS

Status.

Claims 1, 18, 19, and 45 are pending and under consideration with entry of this amendment, new claim 45 being added herein. It is noted that claims 2-17 are withdrawn from consideration subject to an election of species. Accordingly, per MPEP §809.02(c), to the extent all species fall within the limitations of a generic claim ultimately determined to be patentable the non-elected species should no longer be deemed to be withdrawn and claims to the additional non-elected species should be considered by the Examiner.

Claims 1, 18, and 19 are amended and new claim 45 is added herein. These amendments introduce no new matter. Claims 1, 18, and 19 are amended for clarity to eliminate the "subsequence" language and to provide for sequences that hybridize to the listed sequence or its complement. Support is found at page 5 where nucleic acids are defined as being either single or double stranded. It is known that where a nucleic acid is double stranded, identification of one strand in effect identifies its complement. Support for new claim 45 is found at page 25, line 15.

Applicants note that the amendments provided herein are made solely to address rejections under 35 U.S.C. §112 and not to address rejections in light of the prior art. Applicants expressly state for the record that this amendment does not preclude the use of the Doctrine of

Equivalents as applied by an appropriate court. Applicants are clearly entitled, absent amendments in view of the prior art, to assert claims issue from this application against infringers under the Doctrine of Equivalents (*see, e.g. Warner-Jenkinson Co. v Hilton Davis Chem.* 41 USPQ2d 1865 (1997), *Litton Systems Inc. v Honeywell* Inc. 46 USQ2d 1341 (Fed. Cir. 1998)).

35 U.S.C. §112, first paragraph.

Claims 1, 18, and 19 were rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled. In particular, the Examiner alleged that:

A) The claims read on nucleic acids not related to the 20q amplicon and such "unrelated" nucleic acids would cross-react with unrelated genes;

B) One cannot predict from theoretical considerations which nucleic acids will hybridize with the indicated nucleic acid under stringent conditions; and

C) Claim 19 allegedly reads on a nucleic acid that hybridizes to itself.

Applicants respectfully traverse this rejection by argument and amendment. In particular, Applicants explain below the claims, as amended, recite are directed to nucleic acids that specifically bind to ZABC1 (in the 20q amplicon). In addition, one skilled in the art can readily determine any one of the claimed embodiments without undue experimentation.

A) The claims read on nucleic acids that are specific to ZABC1 (SEQ ID NO: 10).

Contrary to the Examiner's assertion, the claims, particularly as amended herein, do not read on nucleic acids that bear no relation (*e.g.* will not bind to) the 20q amplicon. The claims, as amended herein, read on nucleic acids that specifically bind to ZABC1 (SEQ ID NO: 10) under stringent conditions. The term "specific binding" is recognized by those of skill in the nucleic acid art to refer to a binding reaction that is determinative of the presence or absence or amount of the target in a "sample." Thus, the phrase specifically binds implies that the nucleic acids do not bind to other "non-related" sequences.

Moreover, it is noted that that stringent hybridization conditions will generally not permit relatively short nucleic acids (*e.g.* less than 15 or 20 mer) to specifically hybridize to a

target. Longer nucleic acids (*e.g.* 20 mer, 30 mer or more) that can specifically hybridize are of sufficient length that they can be routinely used as specific probes for ZABC1 (SEQ ID NO: 10) and will generally not hybridize, under stringent conditions, to other nucleic acid sequences.

Finally, it is noted that new dependant claim 45 recites a minimum nucleic acid length of 50 nucleotides. A nucleic acid of 50 or more nucleotides that specifically binds to a sequence of SEQ ID NO: 10 will not be expected to cross-react with sequences unrelated to the 20q amplicon.

Thus, contrary to the Examiner's assertion, the claims, as amended, fairly read on nucleic acids that are "related to" the 20q amplicon and, in particular, related to ZABC1.

B) Nucleic acids corresponding to the claimed invention can be identified with only routine experimentation.

Moreover, it is well accepted that:

> [R]ejection of the claims as broader than the enabling disclosuer is generally not appropriate because [when] one skilled in the art could readily determine any one of the claimed embodiments. MPEP §2164.08.

The Examiner is reminded that to be enabling under §112, first paragraph, a patent must contain a description that enables one skilled in the art to make and use the claimed invention. That some experimentation is necessary does not constitute a lack of enablement; the amount of experimentation, however, must not be unduly extensive.

Whether undue experimentation is required by one skilled in the art is typically determined by reference to eight factors considered relevant to the inquiry: (1) quantity of experimentation necessary; (2) amount of guidance presented; (3) presence of working examples; (4) nature of the invention; (5) state of the prior art; (6) relative skill of those in the art; (7) predictability of the art; and (8) breadth of the claims. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) citing *Ex parte Forman Inc.*, 230 USPQ 546 (BPAI 1986). Moreover, the Federal Circuit has held that routine screening (*e.g.,* screening antibodies for a particular binding specificity) is not undue experimentation. *Id.*

With regard to the Forman factors, it is noted that in the instant case, the claims now under consideration are directed to

> An isolated nucleic acid molecule comprising a polynucleotide sequence that specifically hybridizes under stringent conditions to a sequence or to a complement of a sequence selected from the group consisting of . . . SEQ ID NO: 10. . . .

The claims under consideration are relatively narrow (Forman factor 8), being drawn simply to nucleic acids that specifically hybridize to a particular target sequence (SEQ ID NO: 10). Nucleic acid hybridization is, at most, routine experimentation and it is noted that thousands of nucleic acid hybridizations can be performed in a single experiment (*see, e.g.,* Pinkel *et al.* (1998) *Nature Genetics*, 20(2): 207-211, Wang *et al.* (1998) *Science* 280: 1077-1082, and Winzeler *et al.* (1998) *Science,* 281: 1194-1197 describing hybridizations performed on large arrays of nucleic acids). Thus, relatively little experimentation is required to identify nucleic acids falling within the scope of the claim (Forman factor 1). The state of the prior art (nucleic acid hybridization) is well defined and characterized (*see, e.g.,* Tijssen (1993) *Laboratory Techniques in Biochemistry and Molecular Biology: Hybridization with Nucleic Acid Probes*, Elsevier, New York) thus Forman Factor 5 is met. Nucleic acid hybridization is well characterized (Forman Factors 5 and 6) to the point where nucleic acid hybridizations are often performed by software using database information and giving rise to the term experimentation *in silico* (*see, e.g.* Segovia (1998) *Nature Biotechnology*, 16: 25). The preferred target sequence and working examples in the specification provide sufficient guidance for the practice of the invention (Forman factors 2 and 3) and the level of skill in the art is extremely high (*i.e.* Ph.D.). All of the Forman factors indicate that identification of the claimed nucleic acids requires, at most routine experimentation and the rejection under 35 U.S.C. §112, first paragraph, should therefore be withdrawn.

C) Claims can read on inoperative embodiments.

In addition, the Examiner is also reminded that a claim need not exclude possible inoperable embodiments. As stated by the PTO Board of Appeals:

> It is always possible to theorize some combination of circumstances which would render a claimed composition or method inoperative, but the art-skilled would assuredly not choose such a combination. *Ex parte* Cole, 223 USPQ 94 (BPAI 1983)

Similarly, the Federal Circuit has stated that

> It is not the function of claims to specifically exclude either possible inoperative substances or ineffective reactant proportions. *In re Dinh-Nguyen and Stenhagen*, 181 USPQ 46 (CCPA 1974)

That the claims may allegedly read on some nucleic acids that are not elements of the 20q amplicon does not negative patentability. As indicated such embodiments can be readily identified with only routine screening. Thus, the application teaches how to make and use the invention in scope commensurate with the claims and the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

D) Patentability does not require predicting hybridization kinetics.

Patentability of the claimed invention does not require predicting hybridization kinetics. As indicated above, the salient question is whether or not one of ordinary skill in the art, using the teaching provided in the specification can make and use the claimed nucleic acids without undue experimentation. Using the sequence information provided nucleic acids can be synthesized or isolated that specifically hybridize with ZABC1 under stringent conditions. Such specific hybridization can be verified simply by routine screening and there is thus no need to predict hybridization kinetics.

Moreover, with respect to the Examiner's comments that stringent hybridization conditions vary with sequence (*i.e.* nucleotide composition), it is noted that the term stringent conditions is a term of art used in the field and though hybridization conditions may be optimized, *e.g.* to enhance detection/reduce background, *etc.* those of skill in the art can routinely distinguish stringent from non-stringent conditions. Moreover, the specification, at page 7, particularly exemplified stringent conditions in terms of melting point, solution ionic strength, pH, temperature and the like.

As the determination of stringent hybridization conditions is well known and screening of nucleic acids for hybridization under stringent conditions requires at most routine experimentation, the Examiner's rejection of claims 1, 18, and 19 should be withdrawn.

E) Rejection of claim 19 under 35 U.S.C. §112, first paragraph.

As indicated above, the Examiner' rejected claim 19 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not teach how to hybridize two identical nucleic acids to each other. Claim 1 as amended provides for

> [A[polynucleotide sequence that specifically hybridizes under stringent conditions to a sequence or to a complement of a sequence selected from the group consisting of . . . SEQ ID NO: 10 . . .

Claim 1 now provides for the "complement" language with respect to SEQ ID NO: 10, while claim 19 expressly recites SEQ ID NO: 10. The sequence of claim 19 will clearly hybridize to its complement (the complement of SEQ ID NO: 10 recited in claim 1) and thus the enablement rejection of claim 19 is obviated. Accordingly Applicants request that the Examiner withdrawal the 35 U.S.C. §112, first paragraph, rejection of claim 19.

35 U.S.C. 35 U.S.C. §35 U.S.C. §102(a).

Claims 1 and 18 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by GenBank EST106 (accession no: WO5407, NID g1278138) publicly available April 23, 1996.

Applicants provide herewith a Declaration under 37 C.F.R. §1.131(a) establishing that Applicants invented the claimed subject matter prior to the April 23, 1996 date of the cited reference thereby obviating this rejection. Applicants note that the Declaration is currently unsigned. A signed Declaration will be provided upon an indication of otherwise patentable subject matter.

In view of the foregoing, Applicant believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (415) 576-0200.

Respectfully submitted,

Tom Hunter
Reg. No. 38,498

TOWNSEND and TOWNSEND and CREW, LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
(415) 576-0200

TAH
encl: 1) Petition for 3 month extension of time.
2) Declaration under 1.131
3) Amended figure.

File: DOCUMENT2
Last Saved: 00/00/00 0:00 AM